REMARKS

Pursuant to the entry of the instant amendment, claims 1-11 and 15-19 are presently pending and under consideration. All claims stand rejected on reference and/or non-reference grounds. In an effort to expedite prosecution and simply the issues at hand, Applicants have amended the claims as follows:

- The term "prevention" has been canceled from independent claims 1 and 7 and dependent claim 8.
- Independent claims 1 and 7 have been amended to require a "neuroprotective amount" of active ingredient.
- The active ingredient of independent claim 7 has been restricted to "a hydrogenation product of a frankincense extract and a physiologically acceptable salt of said hydrogenation product".
- Dependent claims 10, 11, and 15 have been amended to reflect the narrowed scope of independent claim 7 from which they depend.
- Dependent claims 12-14 have been canceled.

Support for the amendments presented herewith is found in the specification as originally filed, for example at:

- p. 6, lines 3-7: "Another object of this invention is to provide a medicament which has a high bioavailability at the target organ and, along with an excellent effectiveness in the treatment of cerebral ischemia and cranial/brain trauma, can be used in a particularly advantageous way for treating Alzheimer's disease."
- p. 16, lines 1-3: "The neuroprotective effect of frankincense extract containing boswellic acid on the infarct volume after experimentally induced transient focal cerebral ischemia (apoplexy) was checked as follows."

- p. 17, lines 17-18: "The neuroprotective effect of frankincense extract containing boswellic acid on brain injuries was checked as follows."
- p. 19, lines 3-5: "Hence it has been proved that the medicaments produced according to the invention can reduce the lesion of cerebral tissue and resulting neurological peculiarities on account of a cranial/brain trauma or can prevent such a lesion."

Thus, Applicants respectfully submit that no new matter has been added. However, Applicants reiterate that the instant amendments are presented solely for the purpose of expediting prosecution and should not be construed as Applicants' agreement with or acquiescence to the grounds of rejection previously set forth.

Turning to the outstanding Office Action of August 4, 2008:

Rejections under 35 U.S.C. § 112, First Paragraph

The Examiner rejected claim 1-19 under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for a method of treating Alzheimer's disease, allegedly does not provide enablement for a method of treating and/or preventing cerebral ischemia commensurate with the pending claims. The Examiner's challenge appears to be four-fold:

First, the Examiner objects to the enablement of "prevention", construing the term as an extreme absolute. While Applicants respectfully disagree with the Examiner's narrow interpretation, they have nevertheless canceled the term "prevention" from the pending claims in an effort to expedite prosecution.

Second, the Examiner challenges the enablement of the medicament components set forth in claims 12-14, asserting that "these compounds are not known in the art and Applicant has not provided any spectroscopic or experimental data showing these compounds have Applicant's claimed effect". While Applicants respectfully disagree with the Examiner's characterization and

conclusion, Applicants have nevertheless canceled claim 12-14 in an effort to expedite prosecution.

Third, the Examiner challenges the scope of enablement on the grounds that the level of experimentation necessary to identify a medicament that can be administered in a therapeutically effective dose with an acceptable level of side-effects is unduly high. Applicants continue disagree with the Examiner's characterization of the level of experimentation as "undue" and submit that the instant specification meets the requirement of 35 U.S.C. § 112, first paragraph for objective enablement as follows.

At the outset, Applicants wish to again remind the Examiner that a specification is presumed to be in compliance with the enablement requirement of 112, first paragraph, and that the test of enablement is whether one reasonably skilled in the art could make or use the claimed invention from the disclosures in the specification, coupled with information known in the art, without undue experimentation. It is well settled that a specification need not explicitly describe every aspect of every embodiment encompassed by the claims and, in fact, it is preferred that an applicant omits from a patent specification description of that which is well known in the art. See M.P.E.P. § 2164.01 and *United States v. Telectronics, Inc.*, 857 F.2d 778, 785, 8 USPQ2d 1217, 1233 (Fed.Cir. 1988). Furthermore, the fact that experimentation may be complex does not necessarily make it undue, particularly if the art typically engages in such experimentation. *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 USPQ 1165, 1174 (Int'l Trade Comm"n 1983), *aff'd. sub nom., Massachusetts Institute of Technology v. A.B. Fortia*, 774 F.2d 1104, 227 USPQ 428 (Fed. Cir. 1985). See also *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. In other words, the test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976). There are many factors to be considered when determining whether the specification is enabled and whether any necessary experimentation is "undue". Most importantly, the test for undue experimentation is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount

of guidance with respect to the direction in which the experimentation should proceed.

Thus, Applicants reiterate that is not necessary to describe each and every parameter, such as dosage, route and method of administration, with specificity as such detailed information is either known to one skilled in the art or could be readily obtained without undue experimentation. As noted previously, the prior art, as exemplified by the Gerke (WO02/15916) and Banerjee et al. (US 2005/0192251) references previously submitted, describe the use of the *Boswellia* extracts Sallaki® and H15® for the treatment of inflammatory diseases, thereby establishing that medicinal formulations of frankincense extracts were known in the art at the time of invention. See WO02/15916: p. 1, line 31 to p. 2, line 1; US 2005/0192251: paragraph [0003]. Applicants respectfully submit that one of ordinary skill could readily and routinely extrapolate from the prior art knowledge of these compositions having similar structural, physiological and/or biological activity to discern appropriate and optimum dosages and methods of administering the instantly claimed hydrogenation products of *Boswellia serrata* or frankincense extract, balancing positive outcomes with potential negative side-effects with only routine experimentation. Nevertheless, in an effort to expedite prosecution, Applicants have amended claims 1 and 7 to require the medicament to contain a "neuroprotective amount" of active ingredient. Applicants respectfully submit that what constitutes an effective "neuroprotective amount" of a hydrogenation product of a *Boswellia serrata* or frankincense extract may be readily and routinely calculated, for example by assaying for a reduction in infarct volume, neural lesions, and other neurological peculiarities, using conventional protocols such as those described in the instant specification.

The Examiner's final challenge to enablement centers on Applicants' working examples. In particular, the Examiner dismisses Applicants' experimental data, asserting that "it has not been established that rats are an adequate model for stroke in humans, and there is no evidence that Applicant's claimed invention will have the desired effect in humans."

However, Applicants respectfully submit that it is not necessary to "enable one of ordinary skill in the art to make and use a perfected, commercially viable embodiment" in order to comply

with 35 U.S.C. 112, first paragraph. *CFMT, Inc. v. Yieldup Int'l Corp.*, 349 F.3d 1333, 1338, 68 USPQ2d 1940, 1944 (Fed. Cir. 2003). Nor is an Applicant required to demonstrate an invention is completely safe or to prove clinical efficacy in order to show that a therapeutic process is operable (i.e., enabled) (M.P.E.P. § 2107.01 and § 2107.03). As stated in M.P.E.P. § 2107.01, the "courts have found utility for therapeutic inventions, despite the fact that an applicant is at a very early stage in the development of a therapeutic regimen" or that a therapeutic treatment regimen is not at a stage where it is ready to be practiced on humans. *Cross v. Iizuka*, 753 F.2d 1040, 224 U.S.P.Q. 739 (Fed. Cir. 1985); *In re Brana*, 51 F.3d 1560, 34 U.S.P.Q.2d 1436 (Fed. Cir. 1995). Moreover, it is not within the province of the USPTO to require proof of efficacy in animals prior to granting a patent that encompasses therapeutic methods. In fact, the PTO guidelines are explicit on this point: "Office personnel should not impose on applicants the unnecessary burden of providing evidence from human clinical trials. There is no decisional law that requires an applicant to provide data from human clinical trials to establish utility [i.e., operability & enablement] for an invention related to treatment of human disorders" (M.P.E.P. § 2107.03). The guidelines further state that "[t]he Office must confine its review of patent applications to the statutory requirements of the patent law, and in quoting *In re Brana*, *supra*, that "FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws". *Id*.

Rather, all that is required by the patent laws is that a "reasonable correlation" exist between the scope of the claims and the scope of enablement. In other words, if the art is such that a particular assay or model is recognized as correlating to a specific condition, then it should be accepted as correlating unless the examiner has evidence that the model does not correlate. Even with such evidence, the examiner must weigh the evidence for and against correlation and decide whether one skilled in the art would accept the model as reasonably correlating to the condition. *In re Brana*, 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995).

In the outstanding office action, the Examiner cites to a PCRM Research article from 2003 in support of her assertion that the rodent model of the instant specification is not an

adequate art-accepted model for stroke in humans. However, Applicants wish to point out that "PCRM" or "Physicians Committee for Responsible Medicine" is an activist group that staunchly advocates against the use of animals for educational and research purposes. Applicants direct the Examiner's attention to the enclosed overview from the website of the watchdog organization "Activistcash.com". Therein, PCRM is characterized as a "font of medical disinformation", a fanatical animal rights group having operational and financial ties to other animal activist groups that seeks to remove eggs, milk, meat, and seafood from the American diet, and to eliminate the use of animals in scientific research. PCRM routinely argues that experiments involving animal subjects "interfere with new drug development", even rejecting the consensus of the respectable medical community by claiming that animal experimentation "leads AIDS research astray." Such pronouncements have led the American Medical Association (AMA) to issue several strong public rebukes, including a formal censure in 1991 "for purposefully misrepresenting the critical role animals play in medical research."

Given their inherent bias, it is not surprising that PCRM finds fault with the current animal models for stroke and concludes there is "an over reliance upon such models". It is also significant to note that the data on which they rely (e.g., citation #19 to Wiebers et al.) dates back to 1990, over 13 years before the priority date of the instant application. Applicants counter this "evidence" with two references that more adequately reflect the current mainstream position on rodent models for stroke: Butcher et al. (Journal of Neuroscience, 1997) and Carmichael et al. (NeurRx, 2005), copies of which are provided herewith. Like Applicants, Butcher et al. utilize a rat model to investigate stroke and cerebral ischemia. The use of the rodent model for stroke is further supported Carmichael et al. which, given its 2005 publication date represents the most current of the available evidence and thus should be afforded the most persuasive weight. Carmichael et al. come to the conclusion that individual rodent stroke models each capture elements of the human disease, noting that with careful attention to size, mechanism, and purpose, selected rodent models can be used to study the major targets of human neuroprotective

therapies (see conclusion).

Thus, Applicants submit that the Examiner's position is in error, that those of skill in the art do indeed accept the rodent models of the instant specification as correlating to a stroke and cerebral ischemia in humans. Given that the experimental results presented herewith conclusively demonstrate that administration of frankincense extracts to rat models of ischemia and traumatic brain injury led to "a marked and significant reduction of the infarct volume" and "marked and significant reduction of the trauma-induced lesions" in comparison with untreated control groups, Applicants respectfully submit that a reasonable correlation exists between the scope of the claims and the scope of enablement and the working examples.

Applicants wish to further point out that the proper standard for compliance with enablement is not absolute predictability but *objective enablement*. In that vein, supporting evidence need not be conclusive but merely *convincing*. Applicants respectfully submit that the compelling data presented in the instant specification and the accompanying literature is sufficiently convincing that one of ordinary skill in the art would not doubt the feasibility of the claimed invention or its application to higher mammals, including humans. Moreover, the *in vivo* successes documented in the Examples of the instant specification clearly outweigh any speculative allegations of unpredictability. Applicants further submit that the "scaling up" of the disclosed procedures for application to other mammals, including humans, is considered routine experimentation well within the purview of one of ordinary skill. Thus, given the explicit disclosure in the specification of specific *in vivo* working examples, using models that reasonably correlate to higher mammals, including humans, Applicants respectfully submit that one reasonably skilled in the art would be able to make and use invention without undue experimentation.

Thus, for the reasons given above, Applicants respectfully submit that one of ordinary skill in the art would be able to both make and use the invention of the pending claims without undue experimentation. Accordingly, Applicants request reconsideration and withdrawal of the enablement rejection in view of the amendments to the claims and the remarks herein.

Rejections under 35 U.S.C. § 102

Claims 1, 3, 4, 7-9, and 16-19 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Etzel et al. (USPN 5,720,975) (hereinafter referred to simply as "Etzel").

According to the Examiner, Etzel teaches a method of treating Alzheimers's disease comprising administering to a patient in need thereof an effective dosage of the medicament comprising at least one of the following: incense (olibanum), incense extract, biologically active substances contained in incense and boswellic acid (Abstract and col. 1). The Examiner thus concludes that Etzel anticipates the invention of the pending claims.

Applicants respectfully disagree with the Examiner's characterization of the Etzel reference as anticipating. Applicants further submit that the claim amendments presented herewith in order to expedite prosecution render moot the Examiner's assertion of anticipation.

It is well settled that in order for a reference to anticipate, it must disclose each and every element of the pending claims. With respect to claims 1 *et seq*., while Etzel arguably discloses method of treating Alzheimer's disease, there is no mention of treating cerebral ischemia with a hydrogenation product of *Boswellia serrata* in accordance with the method of claim 1. In that Etzel fails to disclose each and every element of claim 1, it cannot serve to anticipate claims 1, 3 or 4. With respect to claims 7 *et seq*., while Etzel arguably discloses the use of frankincense extracts *per se* in the treatment of Alzheimer's disease, there is no mention of treating Alzheimer's disease with a hydrogenation product of a frankincense extract in accordance with the method of claim 7. Importantly, hydrogenation products of frankincense extract are structurally and chemically distinct from frankincense *per se*. Applicants direct the Examiner's attention to the Gerke reference (WO02/15916) mentioned above and its priority disclosure, DE-A 100 41 217, both of which are cited in the instant specification at p. 5, second paragraph, and incorporated therein by reference, wherein hydrogenated products of boswellia are amply

described and defined. Thus, in that Etzel fails to disclose each and every element of claim 7, it cannot serve to anticipate claims 7-9, and 16-19.

Thus, Applicants respectfully request reconsideration and withdrawal of the outstanding rejections of claims 1, 3, 4, 7-9, and 16-19 under 35 U.S.C. § 102(b) in view of the amendments and remarks herein.

Rejections under 35 U.S.C. § 103

Claims 1, 3-11, and 15-19 stand rejected under 35 U.S.C. § 103(a) as being obvious over Etzel et al. (USPN 5,720,975, hereinafter referred to simply as "Etzel") in view of Badria et al. (Z. Naturforsch, Jul-Aug 2003, referred to hereinafter simply as "Badria").

According to the Examiner, Etzel describes the use of incense resins derived from a variety of sources, including *Boswellia* plants such as *Boswellia serrata* and *Boswellia carterii*. The Examiner cites to the Badria reference in support of the assertion that the *Boswellia carterii* resin intrinsically contains 3-oxo-tirucallic acid, 3-hydroxy-tirucallic acid, beta-boswellic acid and 11-keto-boswellic acid. The Examiner thus concludes that it would have been obvious to one of ordinary skill in the art to modify the source of the boswellic acid to arrive at the invention of the pending claims.

At the outset, Applicants wish to point out that the Badria reference is not in fact prior art to Applicants' invention. The instant application is a Rule 371 National Phase Application of PCT/EP04/02839, which, in turn, claims priority to DE 103 11 920.5 (March 18, 2003), DE 103 11 921.3 (March 18, 2003), and DE 103 31 750.3 (July 14, 2003). Publication of the Badria reference occurred after Applicants' priority date, in July-August of 2003. Thus, since the Badria reference is not in fact prior art to Applicants' invention, it should not be used to support a finding of inherency or obviousness.

In any event, Applicants reiterate the arguments above and respectfully submit that Etzel, alone or in combination with Badria, fails to disclose or fairly suggest treating cerebral ischemia

in accordance with the method of claim 1 or treating Alzheimer's disease with a hydrogenation product of frankincense extract in accordance with the method of claim 7. As such, it cannot support a finding of obviousness.

Thus, Applicants respectfully request reconsideration and withdrawal of the outstanding rejections of claims 1, 3-11 and 15-19 under 35 U.S.C. § 103(a) in view of the amendments and remarks herein.

CONCLUSION

The outstanding Office Action set a three-month shortened statutory period for response; accordingly, response is initially due on or before November 4, 2008. Accordingly, Applicant submits that this response is timely and that no additional fee is required. However, in the event that further fees are required to enter the instant response and/or maintain the pendency of this application, the Commissioner is authorized to charge such fees to the undersigned's Deposit Account No. **50-2101**.

If the Examiner has any questions or concerns regarding this communication, she is invited to contact the undersigned.

Respectfully submitted,

Date: November 3, 2008

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